

**REMARKS**

Claims 10-13, 15, and 19-24 are currently pending. Claims 10, 19 and 24 are amended herein. Applicants respectfully request entry of the amendments, as they will place the claims in condition for allowance and/or place the claims in better form for appeal, if necessary.

To facilitate prosecution, and without acquiescing to the Office's rejection, Applicants have amended claims 10 and 19 to remove the phrase "at least one of." As currently amended, claims 10 and 19 recite, "an alkali metal salt or an alkaline earth metal salt." Support for this amendment can be found on page 7, lines 12-15. Claim 10 has been further amended to recite "an amino acid" to make the language of claim 10 consistent with that of claim 19, part (b). Finally, claim 24 was amended to remove the term "precursor." This amendment should overcome the Office's 35 U.S.C. § 112, ¶ 2 rejection of claim 24.

Applicants acknowledge with appreciation that the Office has apparently withdrawn the 35 U.S.C. § 112, ¶ 2 rejection of claim 10, since this rejection was not maintained in the Final Office Action dated September 6, 2006.

**Claim Rejections Under 35 U.S.C. § 112 ¶ 2**

The Office rejected claim 24 because the term “precursor” is allegedly indefinite and lacks an antecedent basis in claim 15. Office Action, page 6. To facilitate prosecution, and without acquiescing to the rejection, claim 24 has been amended to remove the term “precursor.” Thus, Applicants respectfully request that the indefiniteness rejection of claim 24 be withdrawn.

**Claim Rejections Under 35 U.S.C. § 112 ¶ 1**

The Office maintained the rejection of claims 10, 15, and 19 as allegedly lacking enablement for “all claimed possible alkali and alkaline metals and all amino acids.” Office Action, page 6. The Office contends that the claims are only enabled for glycine and sodium salt, since the specification only provides data for these precipitants. Specifically, the Office argues “there could be many potential candidates of amino acids or metals, which are used in the method. Thus, the art is unpredictable, since undue experimentation would be necessary to characterize all possible amino acids and the metals claimed.” Office Action, page 4.

Applicants traverse and respectfully submit that the Office has failed to establish a *prima facie* case of nonenablement, because the rejection is based on a far too stringent standard.

The seminal case of *In re Wands*, 858 F.2d 731, 737-8, cited in the MPEP at § 2164.01, provides a classic example of an enabled invention in a biotechnology field the court considered potentially unpredictable, that of a monoclonal antibody for a

particular antigen. The court acknowledged in *Wands* that the methods required to make hybridoma cells at the time of the invention were complicated and time-consuming and that the outcome of screens to find the claimed monoclonal antibodies would not be predictable. But, the court recognized that despite the unpredictability, hybridoma technology involves a series of routine procedures and that the specification provided sufficient directions for one to proceed. The court's opinion emphasized that, even in an unpredictable art, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.* at 140 (citations omitted). Thus, the test for enablement is not quantitative, but rather, whether the experimentation required to practice the claimed invention is undue. MPEP § 2164.06.

Furthermore, *In re Angstadt* held that generic claims in an unpredictable art are acceptable. 537 F.2d 489, 190 U.S.P.Q. 214 (C.C.P.A. 1976). The question in *Angstadt* was whether a claim generically reciting a "catalyst" was enabled, or whether only the specific catalysts used in the patent's text were enabled. The court explained, "The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by the claim. To require such a complete disclosure would apparently necessitate a patent application or applications with 'thousands' of examples or the disclosure of 'thousands' of catalysts . . . such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from

filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed.” *Id.* at 218 (emphasis in original)(footnote omitted). Thus, the court held that the patent’s disclosure was sufficient to point an experimenter toward appropriate ingredients falling within the generically claimed class.

In view of the foregoing analysis, Applicants respectfully submit that the Office has not met its burden to explain why the claimed procedures would allegedly be undue to one of ordinary skill in the art.

First, the Office acknowledges that the level of skill in the art at the time of filing was high. Office Action, page 5. The fractional precipitation and optimization techniques involved in determining whether an amino acid, alkali, or alkaline metal salt meets the functional requirements of claims 10 and 19 are routine in the art and involve experiments described in the working examples of the specification. For example:

- Choice and preparation of starting material, described on pages 6-7 of the specification;
- Method for obtaining the concentrate of the invention by precipitation, including particular concentration ranges of precipitants, described on pages 7-9;
- Example 1 (specification at pages 9-11), which teaches fractional precipitation of the vWF/FVIII:C concentrate, analysis of the precipitates for vWF:RCoF activity (which measures the functional activity of vWF), and measurement of vWF:Ag and FVIII:C concentrations;

- Example 2 (specification at pages 11-14), which teaches a first and a second precipitation, each precipitation followed by a measurement of vWF activity;
- Example 3 (specification at pages 14-16), which teaches precipitation of the vWF/FVIII:C fraction with the same NaCl/glycine concentration, but with varying addition and incubation times;
- Example 4 (specification at pages 16-18), which teaches fractional precipitation of the vWF/FVIII:C concentrate and, at the same time, teaches a first and second precipitation;
- Example 5 (specification at pages 18-21), which teaches stabilization, sterilization, and lyophilization of a fraction enriched with high molecular weight vWF multimers, and the production of a vWF/FVIII:C concentrate in which the vWF high molecular weight markers were reduced; and
- Example 6 (specification at page 22), which demonstrates fractional precipitation of high molecular weight vWF multimers from a supernatant containing recombinant FVIII:C and plasma vWF.

Thus, as in *Wands*, the high level of skill in the art and the large amount of guidance provided in the specification demonstrate that the amount of experimentation required to practice the claimed invention would not be undue.

Second, the number of precipitants covered by the claims is not unlimited and, thus, does not require undue experimentation. Presently, only six alkali metals (Li, Na, K, Rb, Cs, and Fr) and six alkaline earth metals (Be, Mg, Ca, Sr, Ba, and Ra) are known. Thus, the claimed genus is not so broad as to require undue experimentation to

test the limited number of claimed metal salts. While the number of claimed amino acids is somewhat larger than the twelve claimed metal salts, this does not prevent one of skill in the art to determine the combination of amino acid and alkali metal or alkaline earth metal salts that result in an increased content of functional, high molecular weight vWF multimers, particularly given the abundance of guidance provided by the specification. As in *Angstadt*, the instant specification provides sufficient guidance for the species falling within the claimed genus.

Therefore, since no undue experimentation is required, Applicants respectfully request that the Office withdraw the rejection of claim 10 and its dependent claims 15 and 19, for allegedly failing to enable “any amino acid and/or any alkali or alkaline metal salt.” Office Action, page 4.

The Office also maintained the rejection of claim 15 as allegedly lacking enablement because “specific teachings regarding stabilization of the concentrate product produced during the claimed process are not pointed out in the specification or defined in the claims, since concentrations or necessary conditions are not provided for sucrose, glycine, calcium ions, or albumin” Office Action at page 6. Applicants respectfully traverse.

The specification provides exemplary stabilization conditions with sucrose and glycine (page 10, lines 1-3), and with albumin (page 18, lines 35-37 and page 21, lines 1-3). Furthermore, stabilization is a well-known technique and other embodiments were known in the art at the time of filing the instant application. For example, U.S. Patent No. 6,239,261 to Heimburger et al., cited by the Office in the Action dated August 25,

2005, teaches stabilization conditions with calcium, sucrose, and glycine (column 5, lines 4-14), and with sucrose and glycine (column 5, lines 55-59). Thus, given the general knowledge of stabilization techniques and the specific examples described in the specification, the claimed invention is fully enabled. Limiting claim 15 to specific stabilization conditions is unnecessary, as undue experimentation would not be required to practice the instantly claimed invention.

In view of the foregoing discussion, Applicants respectfully request that the Office withdraw the enablement rejection of claim 15, for allegedly failing to recite stabilization conditions.

### **CONCLUSION**

In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is enabled and definite. Applicants therefore request the entry of this Amendment, the Office's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

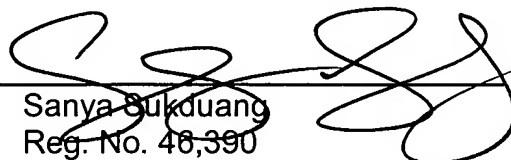
Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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